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Perianal Langerhans cell histiocytosis: a rare presentation in an adult male

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ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare disease characterized by a proliferation of cells that show immunophenotypic and ultrastructural similarities with antigen-presenting Langerhans cells of mucosal sites and skin. LCH in adults is rare, and there are still many undiagnosed/misdiagnosed patients. We describe LCH involvement of the perianal region of a 33-year-old male with a previous history of diabetes insipidus. The differential diagnosis and all the reported cases of LCH of the perianal skin involvement since its description in 1984 till 2016 are discussed. LCH should be considered in the differential diagnosis of perianal ulceration, especially in young patients where topical drug treatment has failed. The history of previous central diabetes insipidus of unknown etiology demands imaging studies in order to rule out central involvement of the disease.

Keywords
Histiocytosis, Langerhans-Cell, Adult, Skin Diseases

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare disease characterized by a proliferation of cells that show immunophenotypic and ultrastructural similarities with antigen-presenting Langerhans cells of mucosal sites and skin.[1] The clinical presentation of LCH is heterogeneous, ranging from mild disease with self-healing solitary lesions to multisystem disease with fatal dissemination. Localized disease, defined as single-system LCH (SS-LCH), most commonly affects the bone, skin, or lymph nodes; and, unlike multisystem disease, has a high rate of both spontaneous remission and favorable outcome (low-risk disease). In contrast to childhood LCH, the most common organ involved in adults is the lung, followed by bone and skin.[2] The skin lesions vary and may appear as scaly, greasy rashes; small, erythematous papules; red or purple nodules, ulcerations, and abscesses.[3-5] The cutaneous lesion may be the sole manifestation of LCH.[6] The histopathology of the lesions is characterized by the presence of LCH cells that are 12–15 μm in diameter with abundant eosinophilic cytoplasm. The nuclei of LCH cells are irregular with prominent folds and grooves, fine chromatin, and indistinct nucleoli.[1] Background eosinophils, lymphocytes, histiocytes, and neutrophils are often present in variable quantities.[1] LCH typically showed CD1a, S100 protein, and langerin expression.

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CASE REPORT

A 33-year-old male attended the medical consultation complaining of a painful perianal lesion over the last 18 months. Previous therapeutic attempts, including different antibiotics orally or topically administered, and topical steroids failed to result in a cure. The patient had a history of central diabetes insipidus 4 years ago, the etiology of which has remained unknown. The diagnosis of diabetes insipidus was based on clinical grounds as imaging studies were not available. The symptoms presented as thirst, polyuria (diluted urine), antidiuretic hormone defect, and a favorable response to desmopressin. On examination, the surgeon reported a perianal ulcerative plaque with necrotic floor and raised edges that was oozing pus. A biopsy was taken. The ulcer was single and measured 2.0 × 2.0 cm with irregular outlines. A histopathological examination of the lesion showed a partially ulcerated epidermal covering, and the underlying dermis was infiltrated by sheets of dyscohesive round cells with reniform nuclei and nuclear infolding (Figure 1A-C). The background showed eosinophils, lymphocytes, and plasma cells. These dyscohesive cells were negative for pan-cytokeratin (CK), and leucocytic common antigen (LCA) (Figure 1D) with diffuse positivity for CD1a (Figure 2A), S100 protein (Figure 2B), and langerin. The histological (morphology and immunohistochemical profile) examination was consistent with LCH of the perianal region.

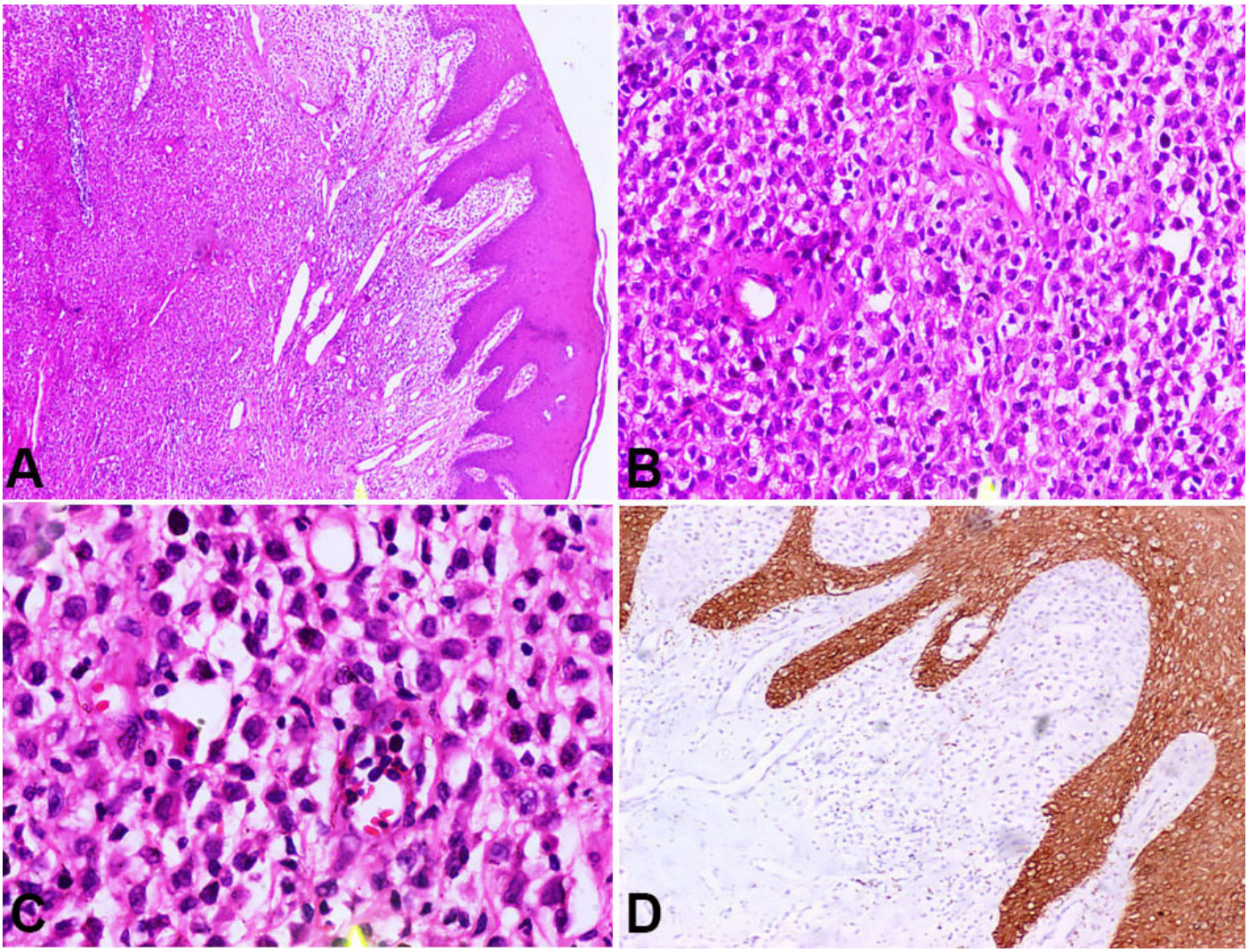

Figure 1. Photomicrography of the biopsy specimen. **A** – Normal epidermal covering with underlying dermal infiltration by sheets of dyscohesive round cells (H&E, 40X); **B** and **C** – The individual cell infiltrate showed reniform vesicular nuclei and visible nucleoli (H&E, 200X and 400X, respectively); **D** – The infiltrate was negative for cytokeratin with positive staining of epidermis as an internal control (200X).

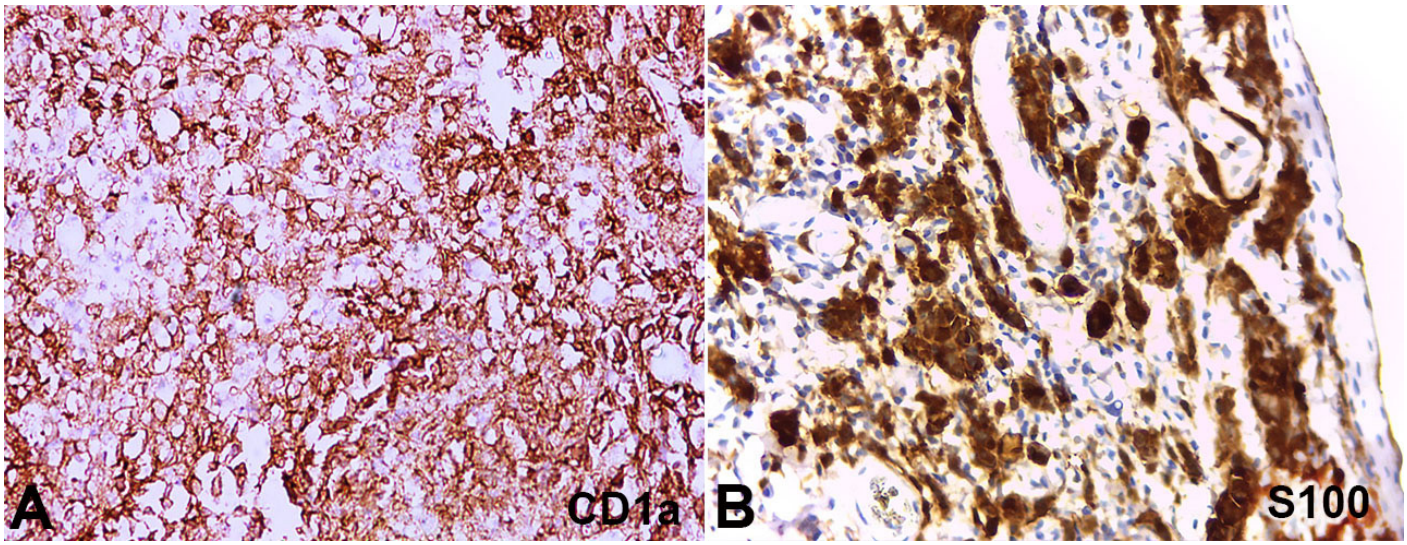

Figure 2. Photomicrography of the biopsy specimen. **A** – Diffuse membranous expression of CD1a (200X); **B** – Diffuse cytoplasmic and nuclear expression of S100 protein (200X).

The study was approved by the Research Ethical Committee of Menoufia University, and the patient signed a written consent regarding the publication of this case report.

DISCUSSION

The diagnosis of LCH was based on the typical histological features and diffuse positivity for CD1a, S100 protein, and langerin. The current investigated case affected an adult male, which, regarding his age, was quite unusual since LCH mostly involves children aged 1–4 years. The disease is more common in males with a male-to-female ratio of 2:1.[7] LCH involving the perianal skin is rare. Searching the databases PubMed and Google using the keywords LCH and perianal lesion during the period between 1984 and 2016, we retrieved 16 cases reported in the English literature (Table 1).[6,8-22] In this review, only one patient was a woman.[22] The age range varied between 14 months and 70 years.[13,15,22] Perianal affection was the only presentation of the disease without systemic involvement in two cases, which were similar to our case.[6,17] In contrast, besides the perianal involvement, bone,[8,10-22] liver,[19] and lung[9,18,19] were concomitantly affected by the disease.

The prognosis of LCH varies according to the type of the disease. Localized types present a better prognosis compared with multi-organ system involvement.[12] Our patient was an apparently healthy man with no evidence of recurrence or systemic involvement till the last follow-up. However, he was previously diagnosed with diabetes inspidus, which was also reported in other studies[9,12,17,21] as a manifestation of LCH in the pituitary gland. Histiocytic infiltrate of the pituitary gland is responsible for the development of diabetes inspidus in different histiocytic disorders, including LCH.[23]

Intertriginous and seborrheic areas, such as those behind the ears, the armpits, and scalp, are the most common sites of the skin involved in LCH, which present as pruritic skin lesions similar to seborrheic dermatitis. Acute forms may present as hemorrhagic or even necrotizing plaques in addition to painful, pruritic, scaly, or erosive lesions.[6]

The affection of perianal region clinically may mimic condyloma accuminata or lata, and the differential diagnosis at microscopy should consider lymphoma, signet ring carcinoma, and melanoma, which could be excluded by the immunohistochemical markers. The definitive diagnosis is confirmed by diffuse positivity for CD1a, S100 protein, and langerin (CD 207). The diffuse positivity for S100 protein and langerin expression[24] excluded the diagnosis of indeterminate cell histiocytosis (ICH), which shares many features with LCH, including CD1a positivity. A lack of Birbeck granules by electron microscopy is another characteristic feature of ICH that discriminates it from LCH. Biopsies are generally undertaken due to the failure of repeated topical therapeutic attempts.

Table 1. Reported cases of perianal involvement in Langerhans-cell histiocytosis (English literature)

Study	Age	Sex	Other areas involvement	Treatment
Cavender and Bennet[8]	2.5 y	M	Frontoparietal bone	NA
Bank and Christensen[9]	18 y	M	DI, Bilateral pneumothorax	NA
Moroz et al.[10]	33 m	M	Alveolar bone and gingiva	Prednisone and methotrexate, vinblastine
Kader et al.[11]	4 y	M	Multiple skull lesions Right scapula	Prednisone and methotrexate
Foster et al.[12]	19 y	M	Anterior cranial fossa, DI	Prednisolone, vincristine, mercaptopurine
Usmani et al.[13]	14 m	M	Bone affection of forehead	NA
Sabri et al.[14]	3 y	M	Gingiva and stomach	Prednisone, vinblastine, 6-mercaptopurine
Field et al.[15]	70 y	M	Left tibia	Potassium permanganate and corticosteroid
Mango et al.[16]	34 y	M	NA	Triamcinolone and thalidomide
Oguzkurt et al.[17]	3 y	M	Central DI	Prednisolone and vinblastine
Mittal et al.[18]	45 y	M	Bone and lung	Nitrogen mustard Topical and systemic corticosteroids Topical pentostatin Abdominoperineal resection of the rectum
Akbayram et al.[19]	16 m	M	Liver lung bone	NA
Tinsa et al.[20]	2 y	M	Scalp	Prednisone and vinblastine
Shakoei et al.[6]	20 y	M	none	thalidomide
Kanik et al.[21]	10 y	M	left mandibular ramus, DI	Systemic corticosteroid and vinblastine
Dere et al.[22]	45 y	F	Femur and tibia	Methotrexate
The present study	33 y	M	None	Methotrexate

DI = diabetes insipidus; F = female; M = male; m = months; NA = not available; y = years.

Most of the reported cases were in remission after the use of vincristine,[12] vinblastine,[10,17,20,21] prednisolone, and methotrexate[10,22]; the latter was used in our case. Aggressive therapy, such as an abdominoperineal resection of the rectum and colostomy was also reported.[18]

CONCLUSIONS

LCH should be considered in the differential diagnosis of perianal ulceration, especially in young patients following the failure of the topical treatment. The history of central diabetes insipidus of unknown etiology requires long follow-up and awareness of the possibility of the appearance of LCH elsewhere in the body.

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